

REMARKS

Claims 21-37 are pending in the application, with Claims 27-37 being withdrawn from consideration pursuant to restriction requirement. Claims 21-26 stand rejected. Claims 24-26 are canceled. Claims 21-22 are hereby amended, with support for said amendments being found generally throughout the specification and specifically within pages 2 and 15-17 of the specification (see for instance "Activity assay and inhibition of PDE activity" on page 16). Claims 21-23, as amended, thus now stand pending.

Claim Rejections –

1. **35 USC § 112, second paragraph**

Claims 21-26 stand rejected under 35 USC 112, second paragraph, as being indefinite, specifically for lack of certain method steps in Claim 21 and a typographical error in Claim 22.

Applicants have amended Claim 21 to include and claim the measuring and correlating method steps. Applicants have also amended the typographical error in claim 22. Applicants therefore respectfully submit that Claims 21-23, as herein amended, are proper and respectfully submit that the 112, second paragraph rejection be withdrawn.

2. **35 USC § 103(a)**

A) Claims 21-26 stand rejected under 35 USC 103(a) as being unpatentable over Frenette (WO 00/64874). The Examiner alleges Frenette teaches (pg 2) the existence of multiple PDE4's raises the prospect of obtaining inhibitors that are selective for individual isoforms of PDE4, thus increasing the specificity of action of such inhibitors, as well as treating arterial sclerosis/atherosclerosis (pg 11). The Examiner acknowledges that Frenette does not teach screening and identifying modulators of PDE4D, but that same would be obvious in light of Frenette's alleged teaching of obtaining inhibitors with regard to PDE4. Applicants respectfully traverse and overcome said rejection.

Contrary to the Examiner's assertion, Frenette at best discloses inhibitors of PDE4 enzymes, but does not disclose activity of the PDE4 enzymes themselves with the development of any diseases, much less atherosclerosis or stenosis. Frenette does not disclose, teach or otherwise suggest step 1 of Claim 21 (measuring activity of a PDE4 target), nor does Frenette disclose, teach or otherwise step 2 of Claim 21 (administering a compound suspected to be an activator or inhibitor of PDE4 to the PDE4 target). Therefore at least two steps of Applicants claimed invention are not disclosed, taught or even suggested by Frenette. One of ordinary skill in the art arguably would not have even considered Frenette, given that Frenette seemingly does not contain any data showing a connection between PDE4 activity and the development of restenosis or atherosclerosis, respectively.

Therefore, Applicants respectfully submit that Frenette does not teach, disclose nor suggest at least two steps of Applicants' claimed invention and that accordingly Claims 21-23, as amended, are novel and non-obvious. Applicants therefore respectfully request that the 103(a) rejection be withdrawn and that said claims be put into condition for allowance.

B) Claims 21-26 are also rejected under 35 USC 103(a) as being unpatentable over Gretarsdottir (US 2005/0287551 A1) The Examiner alleges Gretarsdottir teaches (para 6, pg 1) that there are least 9 isoforms of PDE4D and the PDE4D gene is involved in the pathogenesis of stroke, possibly through atherosclerosis. The Examiner acknowledges that the reference fails to teach inhibiting restenosis, but that it would be obvious to apply an atherosclerosis compound to restenosis. Applicants respectfully traverse and overcome said rejection.

Applicants respectfully note that the Gretarsdottir (US 2005/0287551 A1) reference relied upon by the Examiner is a continuation-in-part application. With regard to the alleged teaching cited by the Examiner in paragraphs 6-8 and 11 of Gretarsdottir, Applicants respectfully submit that this "teaching" seemingly first appears in the

continuation-in-part application No. 10/419,723 filed on April 18, 2003. The priority date of the present application (April 10, 2003) predates the cited CIP date of Gretarsdottir and as such Gretarsdottir is not proper prior art against Applicant's claimed invention. Accordingly, Applicants respectfully request that the 103(a) rejection be withdrawn and that Claims 21-23, as herein amended, be put into condition for allowance.

No further fee is required in connection the filing of this Amendment. If any additional fees are deemed necessary, authorization is given to charge the amount of any such fee to Deposit Account No. 08-2525.

Respectfully submitted,



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